

WHAT IS CLAIMED IS:

1. A composition comprising a PRO256 polypeptide or agonist or antagonist thereof, in admixture with a pharmaceutically acceptable carrier.

5 2. An article of manufacture comprising:

(1) a composition comprising (a) a PRO256 polypeptide, (b) an agonist of a PRO256 polypeptide, or (c) an antagonist of a PRO256 polypeptide, in admixture with a pharmaceutically acceptable carrier;

(2) a container containing said composition; and

(3) a label affixed to said container, or a package insert included in said container, referring to the use of said composition, in the treatment of a cardiovascular, endothelial, and angiogenic disorder.

10 3. A method for identifying an agonist of a PRO256 polypeptide comprising:

(a) contacting cells and a test compound to be screened under conditions suitable for the induction of a cellular response normally induced by a PRO256 polypeptide; and

15 (b) determining the induction of said cellular response to determine if the test compound is an effective agonist, wherein the induction of said cellular response is indicative of said test compound being an effective agonist.

20 4. The method of Claim 3, wherein the cellular response normally induced by said polypeptide is inhibition of cell proliferation.

25 5. A method for identifying a compound that inhibits an activity of a PRO256 polypeptide comprising contacting a test compound with said polypeptide under conditions and for a time sufficient to allow the test compound and polypeptide to interact and determining whether the activity of said polypeptide is inhibited.

30 6. A method for identifying a compound that inhibits an activity of a PRO256 polypeptide comprising the steps of:

(a) contacting cells and a test compound to be screened in the presence of said polypeptide under conditions suitable for the induction of a cellular response normally induced by said polypeptide; and

(b) determining the induction of said cellular response to determine if the test compound is an effective antagonist.

35 7. The method of Claim 6, wherein the cellular response normally induced by said polypeptide is inhibition of cell proliferation.

8. A method for identifying a compound that inhibits the expression of a PRO256 polypeptide in cells that normally express the polypeptide, wherein the method comprises contacting the cells with a test

compound under conditions suitable for allowing expression of said polypeptide and determining whether the expression of said polypeptide is inhibited.

5 9. A compound that inhibits the expression of a PRO256 polypeptide in a mammalian cell which expresses said polypeptide.

10 10. The compound of Claim 9, wherein said compound is an antisense oligonucleotide.

11. An isolated antibody that specifically binds to a PRO256 polypeptide.

10 12. The isolated antibody of Claim 11, wherein said antibody binds to said polypeptide or specifically binds to an epitope on said polypeptide without substantially binding to any other polypeptide or polypeptide epitope.

15 13. The antibody of Claim 12 which is a monoclonal antibody, an antibody fragment, a single-chain antibody, or a humanized antibody.

20 14. A method for diagnosing a disease or susceptibility to a disease which is related to a mutation in a PRO256 polypeptide-encoding nucleic acid sequence comprising determining the presence or absence of said mutation in said polypeptide-encoding nucleic acid sequence, wherein the presence or absence of said mutation is indicative of the presence of said disease or susceptibility to said disease.

25 15. A method of diagnosing a cardiovascular, endothelial or angiogenic disorder in a mammal which comprises analyzing the level of expression of a gene encoding a PRO256 polypeptide (a) in a test sample of tissue cells obtained from said mammal, and (b) in a control sample of known normal tissue cells of the same cell type, wherein a higher or lower expression level in the test sample as compared to the control sample is indicative of the presence of a cardiovascular, endothelial or angiogenic disorder in said mammal.

30 16. A method of diagnosing a cardiovascular, endothelial or angiogenic disorder in a mammal which comprises detecting the presence or absence of a PRO256 polypeptide in a test sample of tissue cells obtained from said mammal, wherein the presence or absence of said polypeptide in said test sample is indicative of the presence of a cardiovascular, endothelial or angiogenic disorder in said mammal.

35 17. A method of diagnosing a cardiovascular, endothelial or angiogenic disorder in a mammal comprising (a) contacting an anti-PRO256 antibody with a test sample of tissue cells obtained from the mammal, and (b) detecting the formation of a complex between said antibody and a PRO256 polypeptide in the test sample, wherein the formation of said complex is indicative of the presence of a cardiovascular, endothelial or

angiogenic disorder in the mammal.

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18. A method for determining the presence of a PRO256 polypeptide in a sample comprising contacting a sample suspected of containing said polypeptide with an anti-PRO256 antibody and determining binding of said antibody to a component of said sample.

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19. A cardiovascular, endothelial or angiogenic disorder diagnostic kit comprising an anti-PRO256 antibody and a carrier in suitable packaging.

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20. A method for treating a cardiovascular, endothelial or angiogenic disorder in a mammal comprising administering to the mammal a therapeutically effective amount of a PRO256 polypeptide or agonist or antagonist thereof.

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21. The method according to Claim 20, wherein the mammal is human.

22. The method of Claim 20, wherein the human has cardiac hypertrophy, trauma, a type of tumor, or age-related macular degeneration.

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23. The method of Claim 20, wherein the PRO256 polypeptide is administered together with a cardiovascular, endothelial or angiogenic agent.

24. The method of Claim 23, wherein the PRO256 polypeptide is administered in combination with a chemotherapeutic agent, a growth inhibitory agent or a cytotoxic agent.

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25. A method for treating a cardiovascular, endothelial or angiogenic disorder in a mammal comprising administering to the mammal a nucleic acid molecule that encodes a PRO256 polypeptide or agonist or antagonist thereof.

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26. The method of Claim 25, wherein the mammal is human.

27. The method of Claim 25, wherein the nucleic acid molecule is administered via *ex vivo* gene therapy.

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28. A recombinant retroviral particle comprising a retroviral vector consisting essentially of (1) a promoter, (2) nucleic acid encoding a PRO256 polypeptide or agonist or antagonist thereof, and (3) a signal sequence for cellular secretion of the polypeptide, wherein the retroviral vector is in association with retroviral structural proteins.

29. An *ex vivo* producer cell comprising a nucleic acid construct that expresses retroviral structural proteins and also comprises a retroviral vector consisting essentially of a (1) promoter, (2) nucleic acid encoding a PRO256 polypeptide or agonist or antagonist thereof, and (3) a signal sequence for cellular secretion of the polypeptide, wherein said producer cell packages the retroviral vector in association with the structural proteins to produce recombinant retroviral particles.

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30. A method for inhibiting endothelial cell growth in a mammal comprising administering to the mammal a therapeutically effective amount of a PRO256 polypeptide or agonist thereof, wherein endothelial cell growth in said mammal is inhibited.

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31. A method of stimulating endothelial cell growth in a mammal comprising administering to the mammal a therapeutically effective amount of an antagonist of a PRO256 polypeptide, wherein endothelial cell growth in said mammal is stimulated.

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32. A method for inhibiting angiogenesis in a mammal comprising administering to the mammal a therapeutically effective amount of a PRO256 polypeptide or agonist thereof, wherein said angiogenesis is inhibited.

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33. A method for stimulating angiogenesis in a mammal comprising administering to the mammal a therapeutically effective amount of an antagonist of a PRO256 polypeptide, wherein said angiogenesis is stimulated.

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34. A method of inhibiting the protease activity of hepatocyte growth factor activator in a mammal comprising administering to the mammal a therapeutically effective amount of a PRO256 polypeptide or agonist thereof, wherein said protease activity is inhibited.

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35. The method of Claim 34, wherein said mammal has a cardiovascular, endothelial or angiogenic disorder.

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36. A method of stimulating the protease activity of hepatocyte growth factor activator in a mammal comprising administering to the mammal a therapeutically effective amount of an antagonist to a PRO256 polypeptide, wherein said protease activity is stimulated.

37. The method of Claim 36, wherein said mammal has a cardiovascular, endothelial or angiogenic disorder.

38. The method of Claim 37, wherein said cardiovascular, endothelial or angiogenic disorder is

5 peripheral vascular disease, hepatic or renal injury or a restinosis disorder.

39. Isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence that encodes an amino acid sequence shown as SEQ ID NO:2.

40. Isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence shown as SEQ ID NO:1.

41. Isolated nucleic acid having at least 80% nucleic acid sequence identity to the full-length coding sequence of the DNA deposited under ATCC accession number 209379.

10 42. A vector comprising the nucleic acid of Claim 39.

15 43. The vector of Claim 42 operably linked to control sequences recognized by a host cell transformed with the vector.

44. A host cell comprising the vector of Claim 42.

20 45. The host cell of Claim 44, wherein said cell is a CHO cell, an *E. coli*, a yeast cell or a Baculovirus infected insect cell.

25 46. A process for producing a PRO256 polypeptide comprising culturing the host cell of Claim 44 under conditions suitable for expression of said polypeptide and recovering said polypeptide from the cell culture.

47. An isolated polypeptide having at least 80% amino acid sequence identity to an amino acid sequence shown as SEQ ID NO:2.

30 48. An isolated polypeptide having at least 80% amino acid sequence identity to an amino acid sequence encoded by the full-length coding sequence of the DNA deposited under ATCC accession number 209379.

49. A chimeric molecule comprising a polypeptide of Claim 47 fused to a heterologous amino acid sequence.

35 50. The chimeric molecule of Claim 49, wherein said heterologous amino acid sequence is an epitope tag sequence.

51. The chimeric molecule of Claim 49, wherein said heterologous amino acid sequence is a Fc region

of an immunoglobulin.

52. An antibody which specifically binds to a polypeptide of Claim 47.

5 53. Isolated nucleic acid having at least 80% nucleic acid sequence identity to:

(a) a nucleotide sequence encoding the polypeptide shown as SEQ ID NO:2, lacking its associated signal peptide;

(b) a nucleotide sequence encoding an extracellular domain of the polypeptide shown as SEQ ID NO:2, with its associated signal peptide; or

10 (c) a nucleotide sequence encoding an extracellular domain of the polypeptide shown as SEQ ID NO:2, lacking its associated signal peptide.

54. An isolated polypeptide having at least 80% amino acid sequence identity to:

(a) the polypeptide shown as SEQ ID NO:2, lacking its associated signal peptide;

15 (b) an extracellular domain of the polypeptide shown as SEQ ID NO:2, with its associated signal peptide;

or

(c) an extracellular domain of the polypeptide shown as SEQ ID NO:2, lacking its associated signal peptide.